AMENDMENT

In the claims

Claims 4, 5, 9-15, 31-34, 43, 44, 47-50, 54, and 98-125 are pending in this application. Claims 4, 31, and 43 are amended as set forth below in the complete listing of the claims, new claims 126-128 are added.

4. (Currently amended) A method of producing a database of data and datapoints for organisms that have not been pre-selected for any particular disease, comprising:

selecting only healthy members of a population of organism not manifesting any disease state;

obtaining data comprising identifying information and obtaining datapoints comprising historical information and data relating to the selected members of the population and their immediate family;

entering the data and datapoints for each selected member of the population into a database, wherein said selected members have not been pre-selected for any particular disease;

associating the respective data and datapoints of the individual member with an indexer; and

storing the database on a computer-readable medium.

5. (Previously presented) The method of claim 4, further comprising:

obtaining a body tissue, body fluid sample, or other biological sample;

analyzing the body tissue, body fluid, or biological sample; and

entering the results of the analysis for each member into the database and associating each result with the indexer representative of each member.

9. (Previously presented) The method of claim 4, wherein the datapoints comprise answers to questions regarding one or more parameters selected from the group consisting of ethnicity, age, gender, height, weight, alcohol intake, number of pregnancies, number of live births, vegetarianism, type of physical activity, state of residence and/or length of residence in a particular state, educational level, age of parent at death, cause of parent death, former or current smoker, length of time as a smoker, frequency of smoking, occurrence of a disease in immediate

family (parent, siblings, children), use of prescription drugs and/or reason therefore, length and/or number of hospital stays, and exposure to environmental factors.

10. (Previously presented) The method of claim 5, wherein the organisms are mammals and the samples are body fluids or tissues.

11. (Previously presented) The method of claim 5, wherein the samples are selected from blood, blood fractions, cells and subcellular organelles.

12. (Previously presented) The method of claim 4, wherein the data comprises phenotypic data from an organism.

13. (Previously presented) The method of claim 4, wherein the data includes one of physical characteristics, background data and medical data.

14. (Previously presented) The method of claim 4, wherein the data comprises genotypic data from nucleic acid obtained from an organism.

15. (Previously presented) The method of claim 14, wherein genotypic data includes genetic markers, non-coding regions, microsatellites, restriction fragment length polymorphisms (RFLPs), variable number tandem repeats (VNTRs), and information indicative of polymorphisms.

31. (Currently amended) A computer system, comprising:

a healthy subject database, wherein:

a healthy subject database comprises data from a population of organisms in which each individual is a healthy subject;

a healthy subject database does not comprise data from a population of organisms that have been pre-selected for any particular disease;

a healthy subject is a subject who does not manifest a disease state; and

the data comprises parameters for subjects in the database; and

a computer comprising software for manipulating the database, wherein the software includes as an executable step determining the frequency of datapoints as a function of a selected parameter in the population.

32. (Previously presented) A system for high throughput processing of biological samples, comprising:

a process line comprising a plurality of processing stations, each of which performs a procedure on a biological sample contained in a reaction vessel;

a robotic system that transports the reaction vessel from processing station to processing station;

a data analysis system that receives test results of the process line and automatically processes the test to make a determination regarding the biological sample in the reaction vessel;

a control system that determines when the test at each processing station is complete and, in response, moves the reaction vessel to the next test station, and continuously processes reaction vessels one after another until the control system receives a stop instruction; and

the computer system of claim 31.

33. (Original) The system of claim 32, wherein one of the processing stations comprises a mass spectrometer.

34. (Original) The system of claim 32, wherein the data analysis system processes the test results by receiving test data from the mass spectrometer such that the test data for a biological sample contains one or more signals, whereupon the data analysis system determines the area under the curve of each signal and normalizes the results thereof and obtains a substantially quantitative result representative of the relative amounts of components in the tested sample.

43. (Currently amended) A method of producing a database <u>of data and datapoints for organisms that have not been pre-selected for any particular common disease</u>, stored in a computer memory, comprising:

selecting only healthy members of a population of organism not manifesting any disease state;

obtaining identifying and historical information and data relating to the selected members of the population;

entering the member-related data into the computer memory database for each selected member of the population<u>, wherein said selected members have not been pre-selected for any particular disease</u>; and

associating the member and the data with an indexer, wherein the database is a relational database.

44. (Original) The method of claim 43, further comprising:

obtaining a body tissue or body fluid sample of an identified member;

analyzing the body tissue or body fluid in the sample; and

entering the results of the analysis for each member into the computer memory database and associating each result with the indexer representative of each member.

47. (Previously presented) The method of claim 4, wherein:

the organisms are selected from among animals, bacteria, fungi, protozoans and parasites and

each datapoint is associated with parameters representative of the organism type and identifying information.

48. (Previously presented) The method of claim 43, further comprising entering phenotypic data regarding each subject.

49. (Previously presented) The method of claim 47, wherein the database ~~that~~ is a relational database and the parameters are the answers to the questions in the questionnaire.

50. (Previously presented) The method of claim 43, wherein the data comprises genotypic data of nucleic acid of the subject, wherein genotypic data includes, but is not limited to, genetic markers, non-coding regions, microsatellites, restriction fragment length polymorphisms (RFLPs), variable number tandem repeats (VNTRs), and information indicative of polymorphisms.

54. (Previously presented) An automated process line, comprising:

a plurality of processing stations; and

the computer system of claim 31.

98. (Previously presented) A combination, comprising the computer system of claim 31 and a mass spectrometer.

99. (Original) The combination of claim 98 that is an automated process line for analyzing biological samples.

100. (Previously presented) A system for high throughput processing of biological samples, comprising: an automated process line comprising a plurality of processing stations, each of which performs a procedure on a biological sample contained in a reaction vessel;

the computer system of claim 31; and

a mass spectrometer.

101. (Previously presented) A method for high throughput processing of biological samples, the method comprising:

transporting a reaction vessel along a system of claim 32, comprising a process line having a plurality of processing stations, each of which performs a procedure on one or more biological samples contained in the reaction vessel;

determining when the test procedure at each processing station is complete and, in response, moving the reaction vessel to the next processing station;

receiving test results of the process line;

automatically processing the test results to make a data analysis determination regarding the biological samples in the reaction vessel; and

processing reaction vessels continuously one after another until receiving a stop instruction, wherein:

the samples tested by the automated process line comprise samples from subjects in the database; and

the computer software enters the data analysis determination into the database.

102. (Previously presented) The method of 101, wherein one of the processing stations comprises a mass spectrometer.

103. (Previously presented) The method of claim 102, wherein the samples are analyzed by a method comprising primer oligo base extension (PROBE).

104. (Previously presented) The method of claim 103, further comprising:

processing the test results by receiving test data from the mass spectrometer such that the test data for a biological sample contains one or more signals or numerical values representative of signals, whereupon the data analysis system determines the area under the curve of each signal and normalizes the results thereof and obtains a substantially quantitative result representative of the relative amounts of components in the tested sample.

105. (Previously presented) The method of claim 103, wherein primer oligo base extension (PROBE) comprises:

a) obtaining a nucleic acid molecule that contains a target nucleotide;

b) optionally immobilizing the nucleic acid molecule onto a solid support, to produce an immobilized nucleic acid molecule;

c) hybridizing the nucleic acid molecule with a primer oligonucleotide that is complementary to the nucleic acid molecule at a site adjacent to the target nucleotide;

d) contacting the product of step c) with composition comprising a dideoxynucleoside triphosphate or a 3'-deoxynucleoside triphosphates and a polymerase, so that only a dideoxynucleoside or 3'-deoxynucleoside triphosphate that is complementary to the target nucleotide is extended onto the primer; and

e) detecting the primer, thereby identifying the target nucleotide.

106. (Previously presented) The method of 105, wherein detection of the extended primer is effected by mass spectrometry, comprising:

ionizing and volatilizing the product of step d); and

detecting the extended primer by mass spectrometry, thereby identifying the target nucleotide.

107. (Previously presented) The method of claim 102, wherein the target nucleic acids in the sample are detected and/or identified by a method, comprising the steps of:

a) hybridizing a first oligonucleotide to the target nucleic acid;

b) hybridizing a second oligonucleotide to an adjacent region of the target nucleic acid;

c) ligating the ~~then~~ hybridized oligonucleotides; and

d) detecting hybridized first oligonucleotide by mass spectrometry as an indication of the presence of the target nucleic acid.

108. (Previously presented) The method of claim 102, wherein the target nucleic acids in the sample are detected and/or identified by a method, comprising the steps of:

a) hybridizing a first oligonucleotide to the target nucleic acid and hybridizing a second oligonucleotide to an adjacent region of the target nucleic acid; b) contacting the hybridized first and second oligonucleotides with a cleavage enzyme to form a cleavage product; and

c) detecting the cleavage product by mass spectrometry as an indication of the presence of the target nucleic acid.

109. (Previously presented) The system of claim 31, wherein the database is a relational database.

110. (Previously presented) The system of claim 31, wherein the datapoints comprise answers to questions regarding one or more parameters selected from the group consisting of ethnicity, age, gender, height, weight, alcohol intake, number of pregnancies, number of live

births, vegetarianism, type of physical activity, state of residence and/or length of residence in a particular state, educational level, age of parent at death, cause of parent death, former or current smoker, length of time as a smoker, frequency of smoking, occurrence of a disease in immediate family (parent, siblings, children), use of prescription drugs and/or reason therefor, length and/or number of hospital stays, and exposure to environmental factors.

111. (Previously presented) The system of claim 31, wherein the organisms are selected from the group consisting of animals, bacteria, viruses, parasites, plants and eubacteria.

112. (Previously presented) The system of claim 31, wherein the organisms are mammals.

113. (Previously presented) The system of claim 31, wherein the data includes information from a biological sample from an organism.

114. (Previously presented) The system of claim 113, wherein the samples are selected from the group consisting of tissues, cells, nucleic acid, blood, plasma, amniotic fluid, synovial fluid, urine, saliva, aqueous humor, sweat, sperm samples and cerebral spinal fluid.

115. (Previously presented) The system of claim 31, wherein the data includes phenotypic data of an organism.

116. (Previously presented) The system of claim 31, wherein the selected parameter is selected from the group consisting of ethnicity, age, gender, height, weight, alcohol intake, number of pregnancies, number of live births, vegetarianism, type of physical activity, state of residence and/or length of residence in a particular state, educational level, age of parent at death, cause of parent death, former or current smoker, length of time as a smoker, frequency of smoking, occurrence of a disease in immediate family (parent, siblings, children), use of prescription drugs and/or reason therefor, length and/or number of hospital stays, and exposure to environmental factors.

117. (Previously presented) The system of claim 31, wherein the data comprises genotypic data of an organism.

118. (Previously presented) The system of claim 31, wherein the data comprises genotypic data from nucleic acid obtained from an organism.

119. (Previously presented) The system of claim 117, wherein the genotypic data includes data selected from the group consisting of genetic markers, non-coding regions,

microsatellites, restriction fragment length polymorphisms (RFLPs), variable number tandem repeats (VNTRs), and information indicative of polymorphisms.

120. (Previously presented) The system of claim 31, wherein the healthy subject database is produced by a method comprising:

selecting only healthy members of a population of organism not manifesting any disease state;

obtaining data comprising identifying information and obtaining datapoints comprising historical information and data relating to the selected members of the population and their immediate family;

entering the data and datapoints for each selected member of the population into the database;

associating the respective data and datapoints of the individual member with an indexer; and

storing the database on a computer-readable medium.

121. (Previously presented) The system of claim 31, wherein the healthy subject database is produced by a method comprising:

selecting only healthy members of a population of organism not manifesting any disease state;

obtaining identifying and historical information and data relating to the selected members of the population;

entering the member-related data into the computer memory database for each selected member of the population; and

associating the member and the data with an indexer, wherein the database is a relational database.

122. (Previously presented) The method of claim 4, wherein the subject database is a relational database.

123. (Previously presented) The method of claim 15, wherein the information indicative of polymorphisms is selected from the group consisting of masses of PCR fragments, peptide fragment sequences, peptide fragment masses, spectra of biopolymers and spectra of small molecules.

124. (Previously presented) The method of claim 50, wherein the information indicative of polymorphisms is selected from the group consisting of masses of PCR fragments, peptide fragment sequences, peptide fragment masses, spectra of biopolymers and spectra of small molecules.

125. (Previously presented) The system of claim 119, wherein the information indicative of polymorphisms is selected from the group consisting of masses of PCR fragments, peptide fragment sequences, peptide fragment masses, spectra of biopolymers and spectra of small molecules.

126. (New) A method of producing a database, consisting essentially of:

selecting only healthy members of a population of organism not manifesting any disease state;

obtaining data comprising identifying information and obtaining datapoints comprising historical information and data relating to the selected members of the population and their immediate family;

entering the data and datapoints for each selected member of the population into a database;

associating the respective data and datapoints of the individual member with an indexer; and

storing the database on a computer-readable medium.

127. (New) A computer system, comprising:

a healthy subject database, wherein:

a healthy subject database consists essentially of data from a population of organisms in which each individual is a healthy subject;

a healthy subject is a subject who does not manifest a disease state; and

the data comprises parameters for subjects in the database; and

a computer comprising software for manipulating the database, wherein the software includes as an executable step determining the frequency of datapoints as a function of a selected parameter in the population.

128. (New) A method of producing a database stored in a computer memory, consisting essentially of:

selecting only healthy members of a population of organism not manifesting any disease state;

obtaining identifying and historical information and data relating to the selected members of the population;

entering the member-related data into the computer memory database for each selected member of the population; and

associating the member and the data with an indexer, wherein the database is a relational database.